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REVIEW



Critical reviews and recent advances of novel non-thermal processing techniques on the modification of food allergens

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ABSTRACT

Nowadays, the increasing prevalence of food allergy has become a public concern related to human health worldwide. Thus, it is imperative and necessary to provide some efficient methods for the management of food allergy. Some conventional processing methods (e.g., boiling and steaming) have been applied in the reduction of food immunoreactivity, while these treatments significantly destroy nutritional components present in food sources. Several studies have shown that novel processing techniques generally have better performance in retaining original characteristics of food and improving the efficiency of eliminating allergens. This review has focused on the recent advances of novel non-thermal processing techniques including high-pressure processing, ultrasound, pulsed light, cold plasma, fermentation, pulsed electric field, enzymatic hydrolysis, and the combination processing of them. Meanwhile, general information on global food allergy prevalence and food allergy pathology are also described. Hopefully, these findings regarding the modifications on the food allergens through various novel food processing techniques can provide an in-depth understanding in the mechanism of food allergy, which in turn possibly provides a strategy to adapt in the reduction of food immunoreactivity for the food industries.

KEYWORDS

Fermentation; modification of food allergens; novel non-thermal processing; pulsed electric field

Introduction

Food allergy has been considered as a significant public health challenge occurring when certain foods are ingested (Blázquez and Berin 2017; Polloni et al. 2017). An epidemiological survey conducted by the World Allergy Organization has reported that approximately 200 to 250 million individuals are suffering from food allergies all over the world (Pawankar et al. 2013). Global analyses have reported that there are approximately 8% of children and 2% of adults suffering from food allergy in developed countries such as United States, Canada, and Italy, and this population number is up to 6% of children and 4% of adults in developing countries such as Brazil and India (Boye 2012; Cianferoni and Spergel 2009; Ekezie, Cheng, and Sun 2018; Gupta et al. 2007). Further, food allergens potentially can trigger severe allergenic reactions, even leading to death, and the prevalence is increasing at a faster rate than any other allergic disorders whereas there is minimal longitudinal research conducted about this phenomenon (Sicherer and Sampson 2010; Wu et al. 2012). It has been reported that more than 170 food types can induce an abnormal immunological response, of which specific foods (including milk, seafood, egg, peanut, soy, tree nut, and wheat) are accountable for 90% of the reported cases (Shriver and Yang 2011). Therefore, food allergy is becoming a global challenge affecting the daily life of individuals.

In order to solve this global challenge related to human health, many studies have been performed to evaluate the relationship between food processing and food immunoreactivity. Most food allergens are proteins, and hence many studies have tried to modify their functional properties by changing the structural properties, which may affect the immunoreactivity of related food proteins. Thermal processing methods, such as boiling and roasting, are considered as the most effective method to alter food attenuation and mitigate allergens by various modifying reactions, including hydrolysis and denaturation of peptide bonds, restructuring disulfide bonds and interaction with other ingredients (Ekezie, Cheng, and Sun 2018). However, the organoleptic properties and nutrient compositions of food products would be affected under thermal treatment, such as protein denaturation of eggs or milk, caramelization resulting from sugar dehydration, gas or water vapor generation by baking, enzyme inactivation due to high temperature (Meda, Orsat, and Raghavan 2017; Regier and Schubert 2005). Moreover, some food allergens present in soy, wheat, celery, and tree nuts are heat-stable, causing limited reductions on their immunoreactivity under thermal processing (Besler, Steinhart, and Paschke 2001; Lasekan and Nayak 2016). In comparison to thermal processing, non-thermal processing showed numerous of advantages not only in maintaining the sensory properties (e.g., freshness, flavor, color attributes)

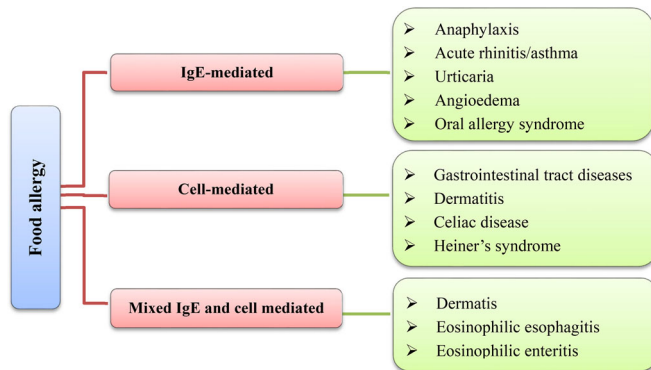


Figure 1. Classification of food allergy.

and improving nutritional properties (phenolics and antioxidants), but also in reducing the food immunoreactivity of soy, peanuts, and shrimp (Li et al. 2011; Li et al. 2013; Meinschmidt et al. 2016).

In this review, we have outlined several types of mechanisms causing food allergies and their related symptoms to provide some necessary information for the readers. Further, we reviewed the recent advances of novel non-thermal processing techniques on the modification of food allergens, including high-pressure processing, pulsed light, ultrasound, cold plasma, fermentation, pulsed electric field, enzymatic hydrolysis, and the combination processing of them. Hopefully, it can provide some strategies for the management of food allergy in the future.

Properties and pathology of food allergens

Most of the allergens present in foods are proteins that are from different families such as pathogenesis-related protein (PR-10), thaumatin-like proteins (TLP), nonspecific lipid transfer proteins (ns-LTP) and profilin (Breiteneder and Mills 2005; Radauer and Breiteneder 2007). Allergens are normally defined as water-soluble proteins (often glycoproteins) with 10–70 kDa, highly resistant to severe food processing conditions, and gastrointestinal digestion (Sicherer and Sampson 2010). Immunoglobulin E (IgE) recognition sites, called IgE-binding epitopes in proteins, can specifically bind with related antibodies resulting in allergic reactions when individuals with allergy history are exposed to the specific allergens (Matsuo, Yokooji, and Taogoshi 2015). IgE-binding epitopes can be classified into two types, including sequential epitopes and conformational epitopes. Sequential epitopes consist of continuous amino acid (AA) sequences, while conformational epitopes are made up of spatially adjacent AAs, distantly located in the AA primary sequence of the proteins (Matsuo, Yokooji, and Taogoshi 2015).

Generally, food allergies can trigger various symptoms ranging from oral allergy syndrome (OAS) to life-threatening anaphylaxis. As shown in Figure 1, food allergies are classified into three categories based on their immunological mechanisms causing allergic symptoms. IgE-mediated food allergy is the first type, which is mediated by IgE antibodies to cause characterized allergenic reactions (Figure 1). IgE-mediated food-induced anaphylaxis usually occurs within

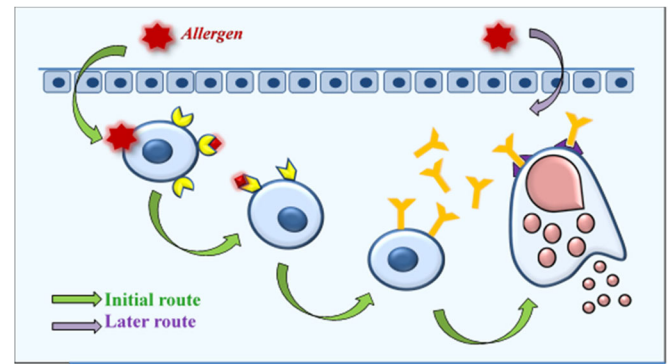


Figure 2. Mechanisms of IgE-mediated anaphylaxis reaction.

2 minutes (Matricardi et al. 2016). The initial phase of IgE-mediated allergy is termed sensitization (Rindsjö and Scheynius 2010). As outlined in Figure 2, allergen enters the body through the epithelial barrier and is taken up by antigen-presenting cells (APC), such as dendritic cells (DC). APCs can induce the differentiation of Th2 cells that are developed from T cells, production of IL-4 and IL-13 from these cells will drive B cell class-switch to the production and secretion of IgE. The secreted allergen-specific IgE will subsequently bind with mast cells in the tissue. When the same allergen is exposed later, the mast cells and basophils are activated and release potent inflammatory mediators (Metcalfe, Sampson, and Simon 2011; Rindsjö and Scheynius 2010). Oral allergy syndrome (OAS) is one of the most common symptoms triggered during IgE-mediated food allergy. Generally, it may involve a sudden onset of itching, stinging pain, and vascular edema of the lips, tongue, palate, and pharynx (Price et al. 2015; Purohit-Sheth and Carr 2005). A typical example of OAS is oral mucosal symptoms that are caused by the intake of the fruits belonging to family Rosaceae (e.g., apple, cherry, peach) among individuals with pollen allergy (Kondo and Urisu 2009; Sloane and Sheffer 2001). It has been reported that oral allergy syndrome responses to a variety of fruits, nuts, and vegetables (Table 1).

The second type is cell-mediated food allergy involving the gastrointestinal tract and occurs when the cell component of the immune system is responsible for the food allergy (Figure 1) (Yu, Liu, et al. 2016b). Clinical manifestations induced by cell-mediated food allergies mostly include food protein-induced enterocolitis syndrome, proctocolitis syndrome, weight depreciation, celiac disease, and pulmonary hemosiderosis (Cianferoni and Spergel 2009; Henderson et al. 2012). Further, in some clinical cases, food allergies can also be triggered by both IgE and immune cells (Figure 1). Mixed IgE-cells mediated food allergy generally induces the cutaneous, gastrointestinal, respiratory diseases, with symptoms such as atopic dermatitis, allergic eosinophilic esophagitis, asthma (Sampson 2003). Atopic manifestations arising from IgE-independent factors mainly include delayed food-allergy-associated atopic dermatitis and eosinophilic gastrointestinal disorders (e.g., eosinophilic oesophagitis), which are often triggered by the allergens in milk (Yu, Liu, et al. 2016b). Cell-mediated and mixed IgE-cell-mediated food allergy can result in predominantly abdominal

Table 1. Symptoms and related allergens causing oral allergy syndrome (OAS) and life-threatening anaphylaxis.

Classification	Symptoms	Allergen sources	References
Oral allergy syndrome (OAS)	Oropharyngeal pruritis (tingling and itching of the lips); Angioedema (involving the oral mucosa, tongue, palate or throat)	Nuts (almond, hazelnut, walnut); Fruits (apple, apricot, banana, cantaloupe, cherry, kiwi, peach, pear, plum, prune, watermelon)	Price et al. (2015) Purohit-Sheth and Carr (2005) Sloane and Sheffer (2001)
Life-threatening anaphylaxis	Lung disease (Heiner syndrome) Gastrointestinal tract diseases (Eosinophilic gastrointestinal disorders, iron deficiency anemia, celiac disease) Rhinoconjunctivitis/Asthma	Milk; Soy; Vegetable (i.e. celery); Fruits (i.e. kiwi); Cereals	Burks et al. (2012)

symptoms (e.g., bloody stools) (Burks et al. 2012). The best strategy for the management of these food allergies is to avoid the intake of those potential allergens.

Effect of novel non-thermal food processing techniques on the food immunoreactivity

In the last decade, minimally processed products gained more attention due to health considerations. In comparison to thermal processing, non-thermal techniques are beneficial to maintain the freshness, flavor, color attributes, and nutritional properties, especially some thermal-unstable compounds such as ascorbic acid and polyphenols. Therefore, novel non-thermal processing techniques show a potential application in the reduction of food immunoreactivity. These techniques generally include high-pressure processing, pulsed light, cold plasma, ultrasound, fermentation, pulsed electric field, enzyme hydrolysis, and their combination (Rahaman, Vasiljevic, and Ramchandran 2016).

High-pressure processing

High-pressure processing (HPP) is also named high hydrostatic pressure processing or ultrahigh-pressure processing. HPP is a non-thermal processing technique, with the pressures generally ranging from 100 to 800 MPa. In the food industry, it is commonly used to inactivate microbes while minimizing the damage in foods, which aims to improve the quality and safety of food products (Khan et al. 2019). The pressures applied to foods are uniform and simultaneous in all directions, whereas the appearance alteration of food-induced by HHP is irreversible due to the compression of air and water (Muntean et al. 2016). Under such a high-pressure condition, the structure of related proteins may be changed. Generally, conformational changes of proteins are observed when the pressure reaches 200-300 MPa (Kurpiewska et al. 2019). Recently, HHP has been considered as a potential application in the reduction of food immunoreactivity due to the denaturation and aggregation of treated protein under high-pressure conditions (Gharbi and Labbafi 2018).

Li et al. (2018) treated soy-protein solutions using HPP (200-500 MPa) for 5-20 min. The results showed that the immunoreactivity of soy protein extract significantly decreased compared to the untreated samples. The highest reduction (55.5%) was observed when the samples were treated with 300 MPa for 15 min. Such reduced immunoreactivity was probably due to the alterations of secondary

and/or tertiary structures of soy allergenic proteins (Rahaman, Vasiljevic, and Ramchandran 2016). Similarly, they also treated 1% soy β -conglycinin solutions with HPP at 200-500 MPa for 5-20 min. The results indicated that the antigenicity reduction of β -conglycinin was up to 92.7%. Related analysis proved that the structural modification of β -conglycinin induced the alteration of the antigenicity under HPP (Xi and He 2018). In walnut, Yang et al. (2017b) processed the walnut samples by different pressures at 250-650 MPa for 5-25 min. The results indicated that the immunoreactivity of walnut to have decreased at 550 and 650 MPa, with a maximum reduction of 46.64%. In ginkgo seed, the protein extract was treated under pressure of 100-700 MPa (Zhou et al. 2016a). Protein immunoreactivity was determined by Western blot and ELISA assay using anti-serum from the mouse; the results found that the immunoreactivity of ginkgo seed protein was completely inhibited when the pressure reached 600 and 700 MPa. This reduction or inhibition in the immunoreactivity can be explained that HPP treatment leads to the structural modification in allergenic proteins, which potentially produces the destroyed or altered IgE-binding sites. These sites have no access to be recognized by IgE antibodies or to elicit immune reactions (Shriver and Yang 2011).

However, some studies have reported that HHP may cause an increase in the immunoreactivity of related food products. Nan et al. (2018) extracted native collagen from bullfrog skin and treated with HHP at 300-500 MPa. They found that the immunoreactivity of treated collagen increased significantly ($P < 0.05$), and such increases had a positive correlation with the increasing pressures. HHP might result in more exposure to collagen antigenic determinant after treatment because of the rise of the random coil region of collagen molecules (Nan et al. 2018). In milk, Meng et al. (2017) isolated and treated bovine β -lactoglobulin (β -Lg) with HPP at 100-500 MPa. The immunoglobulin G (IgG) and immunoglobulin E (IgE) binding to β -Lg were evaluated by the ELISA test with rabbit antibodies and sera from milk-allergic patients, respectively. The results showed that IgG-binding capacities of β -Lg significantly enhanced with increasing pressure, and the IgE binding reached the highest value at 400 MPa. This increase in the immunoreactivity of β -Lg might be attributed to the exposure of IgG linear epitopes after HHP, which resulted in the tertiary structural changes and further influenced the allergenicity of β -Lg (Meng et al. 2017).

It has been reported that high-pressure treatment shows a better performance in maintaining the freshness of foods

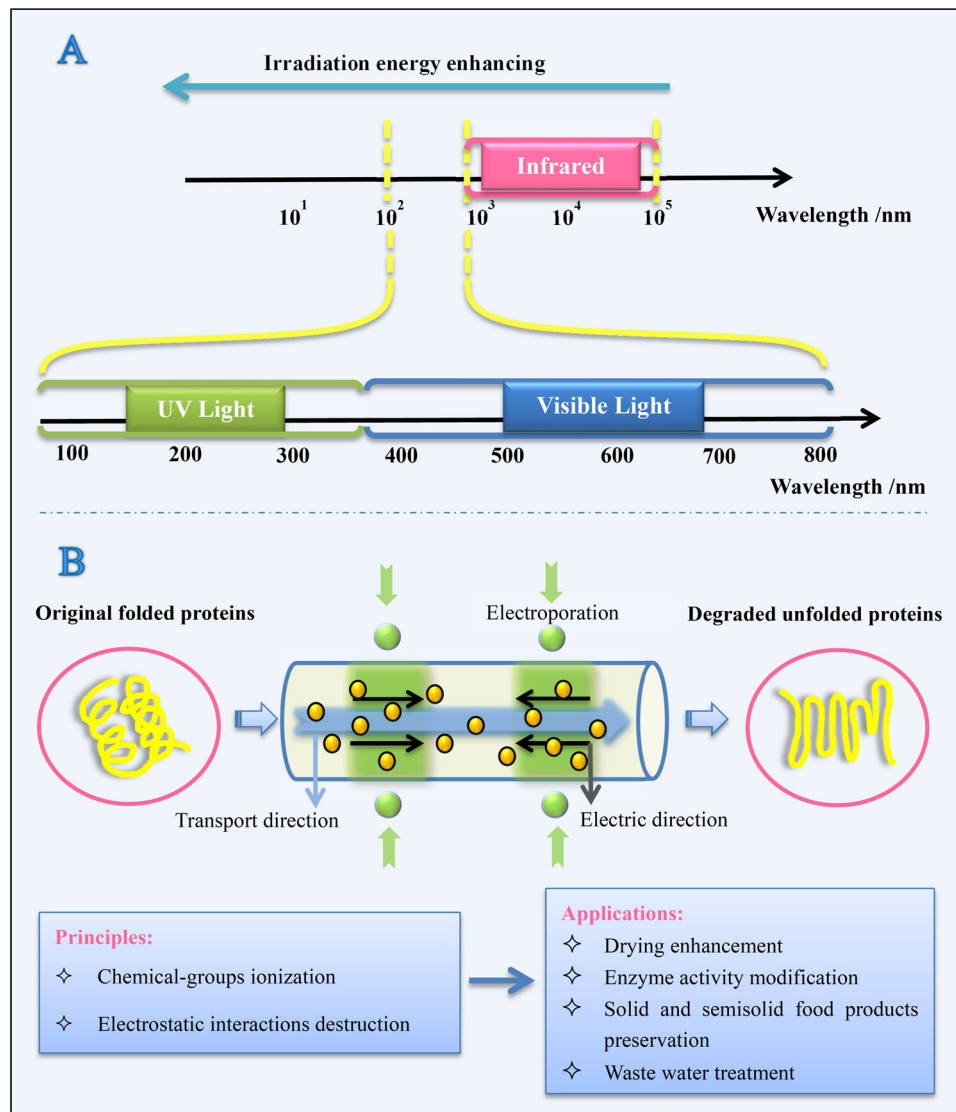


Figure 3. (A) Electromagnetic radiation spectrum of pulsed light; (B) The inactivation process of food allergenic proteins treated by pulsed electric field.

with a minimum impact on the essential compounds, including vitamins, flavor compounds, and pigments (Muntean et al. 2016). Although HHP can reduce food immunoreactivity, it may not affect or even increase the immunoreactivity of food allergens in many cases. Thus, HPP is not a recommended approach until now, and in-depth research in HPP applied to improve food quality and safety is needed in the future.

Pulsed light/pulsed UV-light

Pulsed light (PL) is formed by a sequence of extensively short and high-energy pulses of broad-spectrum white light, which is made up of ultraviolet (UV) light (54%), visible light radiation (26%) and infrared (20%) (Shriver and Yang 2011). The wavelengths of pulsed ultraviolet (PUV) light ranging from 200 nm to 1000 nm can lead to top power pulsed light during a short time (Chung, Yang, and Krishnamurthy 2008a). Accordingly, the intensity of PUV light is thousand-time higher than the conventional continuous UV light (Shriver and Yang 2011). As shown in

Figure 3A, the electromagnetic radiation spectrum of pulsed light is made up of three portions with various light spectrums (Forney and Moraru 2009). In the food system, PUV light can be used to change the conformation of food allergens and induce protein aggregation, potentially leading to the loss of conformational epitopes (Chung, Yang, and Krishnamurthy 2008a; Krishnamurthy, Demirci, and Irudayaraj 2007). However, protein aggregates are also likely to be formed by the re-association of the residual peptides after treatment, which may cause more reactive conformational neo-epitopes and it could further enhance the allergenic potential of foods (Thomas et al. 2007). The inactivation mechanism of PUV light is classified into three categories, including photochemical, photothermal, and photophysical effects, which can cause chemical conversions and protein structure alterations resulting from different heating rates and discontinuous high energy pulse disturbances (Krishnamurthy et al. 2008).

In Table 2, recent studies regarding the effect of UV-light on the food allergens are summarized. In soy, Yang et al. (2010) treated soy extracts with PUV light for 2, 4, and

Table 2. Summary of recent studies on the effect of UV-light processing on food allergens.

Food material	Target allergen	Treatment	Effect on immunoreactivity	References
Milk	α -casein, α -lactalbumin β -lactoglobulin	UV-C treatment (15 min) UV-C treatment (15 min)	α -casein reduced 25% Whey fractions reduced 27.7%	Tamineedi et al. (2013) Tamineedi et al. (2013)
Shrimp	Tropomyosin	PUV sterilization (4 min)	Reduced	Yang et al. (2012b)
Peanut	Ara h 1 Ara h 2 Ara h 3	PUV treatment on butter slurry (1–3 min); Raw and roasted peanuts (2–6 min)	IgE binding of peanut butter slurry reduced up to 6.7 folds; extracts reduced 12.9 folds	Yang et al. (2012a) Yang et al. (2012a) Yang et al. (2012a)
Soy	Gly m5 Gly m6 Soy extracts (i.e., glycinin, β -conglycinin)	PUV treatment (1–6 min) PUV treatment (1–6 min) PUV treatment 2 min PUV treatment 4 min PUV treatment 6 min	Gly m5 reduced 100% Gly m6 retained Reduced by 20% Reduced by 44% Reduced by 50%	Meinlschmidt et al. (2016) Meinlschmidt et al. (2016) Yang et al. (2010) Yang et al. (2010) Yang et al. (2010)
Egg	Ovalbumin Ovomucoid	UV processing(10.6 kJ m^{-2}) UV processing(63.7 kJ m^{-2})	No effect No effect	Manzocco et al. (2012) Manzocco et al. (2012)

6 min, respectively. The results showed that PUV treatment resulted in a downward trend in the number of soy allergens (e.g., glycinin and β -conglycinin) by using indirect ELISA analysis with sera of soy-allergic individuals. IgE binding capacities of soy allergens were decreased by 20%, 44%, and 50% when treated for 2, 4, and 6 min, respectively. This decrease may be due to the aggregation of related allergenic proteins under PUV light (Yang et al. 2010). In peanut, Yang, Mwakatage, et al. (2012a) evaluated the effect of PUV light at different distances (10.8, 14.6, and 18.2 cm) on the IgE binding of raw peanut, roasted peanut, and peanut butter extracts when treated for 1–6 min. The results found that the major peanut allergens, Ara h 1, Ara h 2, Ara h 3 (Figure 4A–C), showed a significant reduction in the intensity of protein SDS-PAGE band with the increase of energy levels ranging from 111.6 to 223.2 J/cm^2 and processing time, while it decreased with the increase in distances away from the PUV light. The ELISA test conducted by human sera reported that the IgE binding capacity of peanut extracts and peanut butter slurry decreased approximately 3 and 7 folds compared with the untreated samples, respectively. The significant reduction in the peanut allergens is attributed probably due to the conversion of peanut protein solubility and the formation of precipitates under PUV radiation (Yang, Mwakatage, et al. 2012a).

A recent investigation demonstrated the immunoreactivity of Gly m5 and Gly m6 in soy was reduced after treating by PUV light at distances of 8 to 10 cm to the light source for 1, 2, 4, and 6 min, respectively. The SDS-PAGE analysis showed that the gel band of Gly m5 subunits completely disappeared after 2-min PUV treatment, while the gel band of Gly m6 retained after 6 min. The loss of bands could be attributed to protein degradation or precipitation (Meinlschmidt et al. 2016). Further, in one study, the IgE binding capacity of major milk allergens (α -casein, α -lactalbumin, and β -lactoglobulin) showed a significant reduction ($P < 0.05$) after a 15-min UV-C treatment (Tamineedi et al. 2013). The immunoreactivity reduction might have resulted from conversions in the discontinuous epitope structures of proteins, and the higher efficiency in reducing whey solution allergens by PUV light treatment may be due to the effect of higher pulses and energy (Anugu 2009; Lee et al. 2001). In addition, Yang, Mwakatage, et al. (2012b) treated raw/boiled shrimp extracts (5 mg/mL) by PUV light

(width: 360 μs , rate: 3/s, distance from the light source: 10 cm). The results showed there was an irreversible reduction in the shrimp allergenic reactivity (Yang, Mwakatage, et al. 2012b). This reduction was associated with the formation of high-weight molecules resulted from the cross-link of tropomyosin and heat-sensitive proteins present in shrimps under PUV light processing (Shriver et al. 2011).

However, Manzocco, Panozzo, and Nicoli (2012) reported that ultraviolet processing could cause both egg white protein aggregation and backbone cleavage, but no significant differences were found in the immunoreactivity of egg white protein compared with the untreated samples. It suggests that these modifications may not change the structure of the epitope present in egg white protein (Manzocco, Panozzo, and Nicoli 2012). So it can be concluded that PUV treatment could reduce allergens in soy, peanut, shrimp, milk, whereas it does not affect allergens in eggs. Although PUV light treatment showed a potential application in the reduction of immunoreactivity of certain foods, which can be used as an alternative processing technique to produce hypoallergic food products; further studies especially clinical tests and in vivo studies are in need to extend the application in the food industry (Vanga, Singh, and Raghavan 2017).

Pulsed electric field

Pulsed electric field (PEF) is considered as an emerging non-thermal technique in the food industry to maintain or even improve food quality. The electric field strength is generally from 0.1 to 80 kV/cm to a specific food located between or passed through two electrodes within certain nanoseconds to milliseconds (Bhat et al. 2019a). The pulsed electric field is not only used to inactive enzymes and microorganisms as commonly known but also applied to modify food protein structure to cause the alterations of functional characteristics (Han et al. 2018). Although the exact mechanisms of PEF processing are not clear, it has been confirmed that PEF leads to the losses and modifications of secondary and tertiary structures of proteins due to the ionization of specific chemical groups or destruction of electrostatic interactions (Wei et al. 2018; Zhao and Yang 2008). Firstly, the specific protein molecules are polarized,

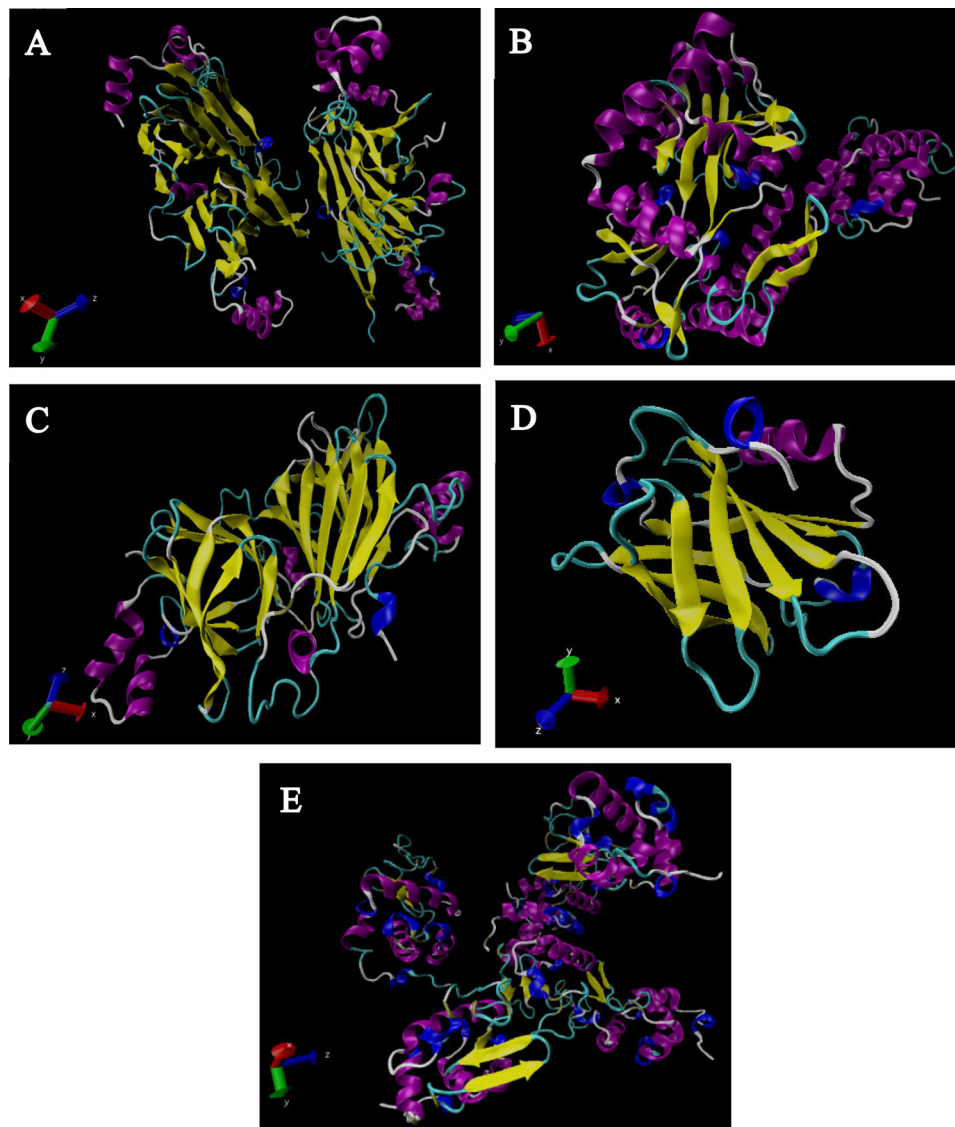


Figure 4. Crystal structures of peanut major allergens: Ara h 1(A), Ara h 2(B) and Ara h 3(C) and milk major allergens: β -lactoglobulin(D) and α -lactalbumin(E) (Source: protein data bank; PDB code: 3S7E, 3OB4, 3C3V, 2Q2M and 1F6S respectively) [α -helix: Purple, 3/10 helix: Blue, π -helix: Red, β -sheets: Yellow, Turns: Cyan, coils: White].

which is followed by the explosion of the hydrophobic amino acids to the solvent. Eventually, unfolding proteins convert into corresponding aggregates under high intensive electric field (Zhao and Yang 2009). The inactivation process of PEF applied to food allergenic proteins is shown in Figure 3B (Bhat et al. 2019b). PEF has attracted increasing attention and expands its applications in the food industry due to the advantages, including energy-saving mode, minimal loss of nutrients, the accessibility of liquid food systems (Han et al. 2018).

Yang et al. (2017a) reported that high-intensity PEF treatment at 25-35 kV/cm for 60-180 μ s significantly altered the conformational structures, such as α -helix and immunogenic properties of ovalbumin present in egg white. Under high strength and long-time duration of PEF processing, the maximum reduction was observed after treatment at 35 kV/cm for 180 μ s (Yang et al. 2017a). Therefore, PEF processing has the potential to decrease the immunoreactivity of ovalbumin. Vanga, Singh, and Raghavan (2015) evaluated

the effect of the oscillating and static electric field (2450 MHz, 0.05 V/nm) at different temperatures (300, 380, 425 K) on the structure of Ara h 6 (a major peanut allergen) using the simulation of molecular dynamics. The result showed that the electric fields induced the alteration of protein structure at these three given temperature conditions, which may further impact its functional properties (Vanga, Singh, and Raghavan 2015). Sequentially, Vanga et al. (2016) treated peanut flour samples using an electric field with intensities of 10, 15, and 20 kV for 60-180 min. The results found the conformational changes in the α -helix structure increased with the rise of processing duration, which might be due to the formation of new random coils and aggregates during processing. However, Johnson et al. (2010) investigated the effect of PEF (electric field strengths: 0-35 kV/cm, frequency: 2 Hz, energy input: 0-130 kJ/kg) on purified allergens including Ara h 2, 6 (peanut 2S albumins) (1 mg/mL) in native peanuts, Mal d 3 (0.5 mg/mL) and Mal d 1 (0.5 mg/mL) in apples. The results demonstrated no

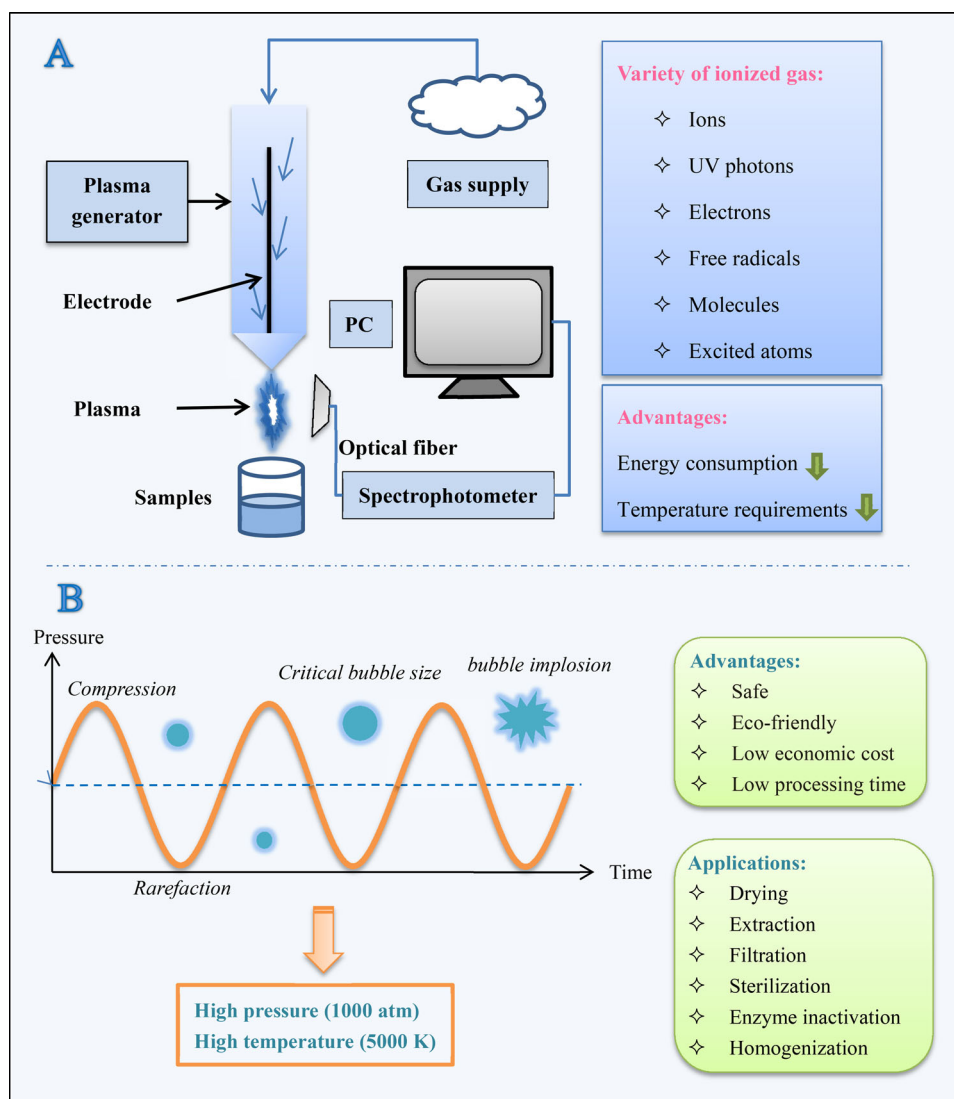


Figure 5. (A) Mechanisms and advantages of cold plasma processing system; (B) Mechanisms and applications of ultrasound processing system.

significant changes were observed in the secondary structures of these allergens after pulsed electric field treatment, which currently could not be accurately explained due to insufficient research analysis (Johnson et al. 2010). In celery, no obvious changes were found in the reduction of allergens after pulsed electric field processing at 10 kV with a frequency of 50 Hz (Paschke 2009). In comparison to thermal processing and other non-thermal treatments, the effect of PEF on the modification of related food allergens is minimal. Therefore, the optimization of processing conditions regarding PEF processing needs further studies.

Cold plasma

Cold plasma is considered as a novel, non-thermal technology which has been mainly used in microbial inactivation and food decontamination due to the less energy consumption and lower temperature requirements compared to the conventional processing methods (Ekezie, Cheng, and Sun 2018). The plasma processing system is mainly made up of a high-frequency plasma generator and ceramic electrode

(Figure 5A) (Chizoba Ekezie, Cheng, and Sun 2018). As the fourth state of matter, plasma is a partially ionized gas consisting of reactive species, such as ions, UV photons, electrons, free radicals, molecules, and excited atoms. These reactive species can interact with proteins and alter their conformations (Ekezie, Cheng, and Sun 2018; Inagaki 2014; Tolouie et al. 2018). Many studies have reported that plasma treatment showed a potential application in the reduction of food immunoreactivity.

Recently, Venkataratnam et al. (2019) treated dry, defatted peanut flour and whole peanut under cold atmospheric plasma with a voltage of 80 kV for various treatment times (0, 15, 30, 45, 60 min). The results revealed the antigenicity reductions of defatted peanut flour and whole peanut were up to 43% by competitive ELISA analysis with bovine serum albumin; the secondary structure modifications were also observed by circular dichroism (Venkataratnam et al. 2019). In one study, tropomyosin, a major shrimp allergen, was treated with direct dielectric discharge cold plasma for 5 min with a voltage and frequency of 30 kV and 60 Hz, respectively. The results showed that the immunoreactivity in shrimp to have reduced 76% after cold plasma treatment

Table 3. Summary of recent studies on the effect of ultrasound processing on food allergens.

Food	Target allergen	Treatment	Immunoreactivity	References
Soy Milk	Proteins	37 kHz, 10 min	Reduced 24%	Choudhary et al. (2013)
	α -casein	500 W and 20 kHz (10–30 min)	No effect	Tammineedi et al. (2013)
	β -lactoglobulin	500 W and 20 kHz (10–30 min)	No effect	Choudhary et al. (2013)
	α -lactalbumin	500 W and 20 kHz (10–30 min)	No effect	Stanic-Vucinic et al. (2012)
Peanut Shrimp	Ara h1,	50 Hz for 5 h	Reduced 84.8%	Li et al. (2013)
	Ara h2	50 Hz for 5 h	Reduced 4.88%	Li et al. (2013)
	Boiled shrimp proteins	30 kHz, 800 W (0–50 °C, 0–30 min)	Reduced 40%–50%	Li et al. (2011)
	Raw shrimp Proteins	30 kHz, 800 W (0–50 °C, 0–30 min)	Reduced up to 8%	Li et al. (2011)
Crayfish	Tropomyosin	100–800 W, 15 min	Reduced	Zhang et al. (2018)
	Shrimp and allergens	30 Hz, 800 W (30–180 min)	Reduced up to 75 %	Li et al. (2006)
	Arginine kinase	200 W, 30 °C (10–180 min)	No effect	Chen et al. (2013)

(Shriver 2011). Similarly, Nooji (2011) utilized the same plasma to wheat for 5 min, and found the reduction of immunoreactivity was up to 37%.

The conformational binding epitope was masked or disrupted by the free radicals generated under the plasma exposure, leading to the removal of IgE-mediated reaction (Nooji 2011). In another study, protein extracts from untoasted soy were treated by direct cold atmospheric pressure plasma (CAPP) for 0–10 min at a peak-to-peak (pp) voltage of 9, 10, and 11 kVpp and a frequency of 3.0 kHz. The result showed that the reduction of Gly m5 (the significant soy allergens) immunoreactivity under CAPP was almost completed as determined by sandwich ELISA utilizing human sera and specific mouse monoclonal anti-Gly m5 antibodies, which might be due to the conformational and linear epitope modification or antibody binding site destruction (Meinlschmidt et al. 2016).

Further, Tammineedi et al. (2013) treated α -casein of milk with cold atmospheric plasma at 13.56 MHz radiofrequency and at a rate of 30.7 L/min of argon gas for 5, 10, and 15 min, respectively. The results demonstrated that no significant changes in food immunoreactivity were observed after cold atmospheric plasma treatments, which might attribute to the low plasma power or indirect exposure of the sample to the cold atmospheric plasma system (Tammineedi et al. 2013). Therefore, the effects of cold plasma on the immunoreactivity of foods are different in various food sources, and the mechanism is not clear, which implies that more related studies are needed. Until now, it is known that cold plasma could decrease allergens in soy, peanut, shrimp, wheat, but there is no difference in allergen amounts in treated milk found. Moreover, many studies have shown cold plasma processing to decrease the quality of food due to lipid oxidation acceleration, reduction in vitamins, and sensory attributes loss during processing (Dasan and Boyaci 2018; Misra et al. 2011; Pankaj, Wan, and Keener 2018). Thus, cold plasma treatment might not be an ideal food processing method, and more novel processing techniques are to be explored.

Ultrasound processing

Ultrasound is specified as sound waves bearing a frequency of up to 20 kHz (Awad et al. 2012). It is considered as one

of the emerging and efficient food processing technologies widely used for different applications, such as homogenization, cutting, extraction, inactivation of microorganisms or enzymes, drying enhancement, surface cleaning, depolymerization (Feng, Barbosa-Cánovas, and Weiss 2011). As shown in Figure 5B, the ultrasound mechanism and cavitation phenomenon are outlined. The sonication bubbles are formed from mechanical waves compressing, refracting intermittently, and collapsing at critical bubble sizes under the application of high energy. The implosion of bubbles results in localized high pressure up to 1000 atm and high temperatures up to 5000 K. These extreme parameters can induce the structural alteration of allergens (Soria and Villamiel 2010).

Table 3 summarizes recent studies on the effect of ultrasound processing on food allergens. In soy, Choudhary et al. (2013) treated soy proteins with high-intensity ultrasound at 37 kHz for 10 min. The results showed the immunoreactivity of soy proteins decreased by 24% compared with the untreated samples, which may attribute to the change of secondary and tertiary conformation in soy proteins (Choudhary et al. 2013). In roasted peanut, studies have reported that the major allergen Ara h 1 and Ara h 2 reduced by 84.8% and 4.88%, respectively, when treated with ultrasound at 50 Hz for 2 h (Li et al. 2013). The reduction in peanut allergens is due to the structural changes of IgE binding epitopes located on the α -helical regions of Ara h 1 and Ara h 2 under the high-intensity ultrasound treatment for a long time duration (Barre et al. 2007; Wu, Lin, and Chau 2001).

Li et al. (2006) treated shrimp and purified shrimp allergen with high-intensity ultrasound at 800 W, 30 Hz for 30–180 min. The results showed that the immunoreactivity of shrimp allergen decreased by up to 75% determined by ELISA with the serum from shrimp-allergic patients and polyclonal antibodies. Moreover, it was observed that there was a linear relationship between protein immunoreactivity and the duration of the treatment (Li et al. 2006). Similarly, Zhenxing, Caolimin, and Jamil (2006) treated peeled shrimp (*Penaeus vannamei*) using ultrasound (30 Hz, 800 W) with temperatures of 0 and 50 °C for 1.5 h. The results showed that shrimp immunoreactivity decreased under the treatment of high-intensity ultrasound at 50 °C. In one study, the major shrimp allergen, tropomyosin (TM), was treated with a high-intensity ultrasound at 100–800 W for 15 min. The

results based on immunoblotting and ELISA tests using patients' sera showed that ultrasound significantly reduced the immunoreactivity of shrimps due to the degradation of TM molecules under high-intensity treatment (Zhang, He, et al. 2018b). However, Chen et al. (2013) treated arginine kinase (AK), a significant shellfish allergen with ultrasound (200 W) at 30 °C for 10–180 min. The results found that ultrasound treatment rarely induced the degradation of crayfish AK and reduction of IgE-binding activity (Chen et al. 2013). Besides, Tammineedi et al. (2013) treated milk proteins using ultrasound treatments at 500-W power and 20-kHz frequency for 10, 20, and 30 min, respectively. No significant differences were observed in the intensity of the SDS-PAGE gel band of α -casein, β -lactoglobulin, and α -lactalbumin (Figure 4D and E), which might attribute to the low intensity and short ultrasound processing time. Similar results targeting the immunoreactivity of cow's milk under ultrasound treatments were also observed in other studies (Choudhary et al. 2013; Stanic-Vucinic et al. 2012; Tammineedi et al. 2013).

Ultrasound processing gained significant attention due to its numerous advantages such as environmental-friendliness, less energy consumption, higher mass transfer rate, and original flavor maintenance of food products during processing (Wang et al., 2019). Moreover, ultrasound processing shows a potential application in the reduction of immunoreactivity in soy, peanut, shellfish, which can be used as alternative non-thermal processing in the future. It is also noticed that ultrasound treatments seem to be more efficient when combined with heat, instead of being used solely. Thus, ultrasound can be considered as an alternative non-thermal processing in the reduction of food immunoreactivity, whereas the optimization of processing conditions is needed (e.g., time duration, frequency, and temperature).

Fermentation treatment

Fermentation is considered as one of the most common techniques in food industry. In nowadays, fermented foods are obtained high attention by the human and play an essential role in the market consumption of daily food. The primary examples are certain protein-abundant foods, such as dairy foods (yogurts, cheeses), alcoholic drinks (wine, beer), fermented vegetables (sauerkraut and pickles), and fermented meats (sausages and salami) (Soccol, Pandey, and Larroche 2013). Fermentation processing is induced by specific microorganisms acting on food substrates. One of the most common examples is that sugars could be converted to alcohol, carbon dioxide, and organic acids under anaerobic conditions. In this process, microorganism strains and related conditions (e.g., temperature, pH, and substrate concentration) significantly affect the specific products liberated (Pérez Díaz, Altuntas, and Juneja 2017). Other than the applications of fermented food products, recent studies have found that the linear and conformational epitopes of allergenic proteins can be modified and destroyed by hydrolysis during fermentation.

Yang et al. (2018) investigated the impacts of solid-state fermentation by mixing yeast, *Lactobacillus casei*, and *Bacillus subtilis* on the immunoreactivity of soy meal (SBM). The results found that the IgE binding capacity of the SBM was significantly reduced after fermentation. This reduction might be due to the degradation of protein into peptides with low molecular weights, which results in the damage of some allergenic sequences of β -conglycinin and glycinin present in soys. Similar results have been observed by Chung, Yang, and Krishnamurthy (2008b), the lower immunoreactivity of soy was found in fermented soy by *Bacillus subtilis* KFCC 11293 and *Lactococcus lactis subsp. lactis* compared with the untreated samples (Chung, Yang, and Krishnamurthy 2008b). Hence, fermentation is effective in the reduction of soy allergens (Yang et al. 2018). Moreover, mixed cultures may have a more significant effect on such processing. In a study, lower immunoreactivity was observed when wheat flour was fermented by cultures-yeast mixtures, compared with by the homo-hetero fermentative lactic acid bacteria. The results might be due to the performance of mixed cultures with strong proteolysis capabilities to induce their broad specificity (De Angelis et al. 2006; Leszczyńska et al. 2009). In milk, Yao et al. (2014) studied the IgE-binding capacity changes of four proteins, including α -lactalbumin (LA), β -lactoglobulin (LG), α -caseins (CN), and β -caseins (CN) during fermentation by *Lactobacillus rhamnosus* GG. The results indicated the IgE-binding capacity of four proteins in fermented milk to have been significantly reduced by up to 70%, which might be due to the alteration of allergens or the cleaving of allergenic protein epitopes (Yao et al. 2014). Besides, Kim et al. (2008) performed a study using a competitive indirect ELISA with human sera to explore the immunoreactivity changes in saeujeot (a variety of shrimp salted and fermented). The saeujeots were fermented with different salt concentrations (25, 15, and 10%) at various temperatures (25, 15, and 5 °C). They found that the IgE-binding capacity of shrimps was significantly decreased when fermented with a low salt concentration at high temperatures. These significant reductions in the immunoreactivity of fermented foods may be due to the hydrolysis and degradation by certain microbes, which in turn can lead to modification or destruction of sequential and conformational epitopes of food proteins and to cause further reduction of food immunoreactivity (Zhou et al. 2016b). In conclusion, a significant reduction can be observed in allergens from soy, wheat, shrimp, and even milk by fermentation treatment. Therefore, fermentation, especially long-time fermentation, shows a potential application in reducing food immunoreactivity.

Enzymatic hydrolysis

Enzymatic hydrolysis treatment has obtained significant attention due to its efficient, selective, reproducible, and environmental-friendly characteristics, and is regarded as a promising technique to produce hypoallergenic foods (Zhang, He, et al. 2018a). In the food processing industry, there are more than 55 enzyme varieties applied during the

processing of related products (Van Oort 2009). Many studies have reported that enzymatic hydrolysis treatment shows a potential reduction in the immunoreactivity of the proteins or their extracts by changing the structure of allergic proteins. The mechanism of this technique is to modify or destroy the linear epitopes of allergens by proteolytic or cellular enzymatic hydrolysis. During processing, the structures of the proteins are broken down into peptides and/or amino acids (Ekezie, Cheng, and Sun 2018; Kasera et al. 2015).

Enzymatic hydrolysis processing technique has been used to produce easy-digested food for infants for over 60 years (Knights 1985). For instance, proteases are often applied to produce hydrolyzed formula milk by hydrolyzing the proteins in milk, which is beneficial to improve the digestibility of milk powder (Fleischer, Venter, and Vandenplas 2016). Further, many studies have found that enzyme treatment can reduce the allergic risk of food. Yu et al. (2011) reported that enzymatic treatment could significantly reduce (up to 100%) the amount of two significant allergens (Ara h 1 and Ara h 2) in roasted peanut kernels. Specifically, the roasted peanut kernels were treated with α -chymotrypsin and trypsin for 1–3 h. The results showed that Ara h 1 and Ara h 2 were hardly determined by the ELISA test with sera (Yu et al. 2011). Similarly, Yu, Goktepe, and Ahmedna (2013) treated peanut butter samples with trypsin, α -chymotrypsin, or the combination of these two enzymes at 37 °C for 3 h or at room temperature for 24 h. The results demonstrated that the immunoreactivity of Ara h 1 and Ara h 2 was reduced by 100% under the combination of α -chymotrypsin and trypsin (1:1) at 0.04% of enzyme-to-peanut butter ratio. Thus, the combination of trypsin and α -chymotrypsin enhanced the efficiency in degrading the Ara h 1 and Ara h 2 compared to one enzyme applied (Yu, Goktepe, and Ahmedna 2013). Beta-lactoglobulin (β -Lg) is a principal component in milk. Duan et al. (2014) divided 24 BALB/c mice into three groups and injected them subcutaneously with native bovine β -Lg and its hydrolysates on days 0, 7, and 14, respectively. The results suggested that the spleen lymphocyte proliferation level of the sensitized mice induced by β -Lg hydrolysates was lower than that of the intact one, which implied enzymatic hydrolysis treatment could reduce the immunoreactivity of β -Lg. The reason for this outcome might be the three-dimensional structure of β -Lg to have been destroyed by the hydrolysis processing, accompanying specific epitopes removed subsequently (Duan et al. 2014). Likewise, Kulis et al. (2012) performed an in vivo test in mice, and the allergenic activity of cashew proteins decreased by pepsin digestion (Kulis et al. 2012). In wheat flour, studies found that the immunoreactivity of gliadin was eliminated when treated with sequential *alcalase-papain* hydrolysis at 53 °C, pH of 8.0 for 62 min (Li et al. 2016). Further, Kasera et al. (2015) investigated that protein extracts from legumes-kidney beans, peanut, and black gram were hydrolyzed by *flavourzyme* and *alcalase*. The results showed that the immunoreactivity of hydrolysates to have been significantly reduced compared to the untreated one (Kasera et al. 2015).

However, enzymatic hydrolysis treatments have conflicting results when evaluating their effects on the immunoreactivity of plant foods, since sometimes it contributes to increasing its immunoreactivity. In lentil protein extracts, studies found that the allergic proteins residual still can be detected using the IgE immunoblotting and the ELISA test with patients' sera when hydrolyzed with *flavourzyme* and *alcalase* (Cabanillas et al. 2010). Palosuo et al. (2003) applied pepsin and trypsin to wheat and found the IgE-binding ability of the ω -5 gliadin (a major allergen in wheat was not affected after digestion. It was probably because hydrolyzed peptides are cross-linked by tissue transglutaminase (tTG) into large allergen complexes, which may increase their potential for eliciting severe immunological responses in sensitized/allergic individuals (Palosuo et al. 2003). Kiyota et al. (2017) observed the reactivity of tomato allergen profilin (Sola I 1) after papain treatment by using competitive indirect ELISA with horse serum; the results showed that Sola I 1 reactivity was retained after treatment (Kiyota et al. 2017). Panda et al. (2015) applied five enzymes (*alcalase*, *trypsin*, *chymotrypsin*, *bromelain*, or *papain*) separately to soy protein isolates by IgE immunoblot evaluation using the sera from eight soy-allergic patients. The results indicated that the enzymatic hydrolysis process had no effect on the immunoreactivity reduction, and *chymotrypsin* or *bromelain* revealed the potential to enhance soy immunoreactivity (Panda et al. 2015). Thus, the application of the enzymatic treatment might be a good alternative to decrease the immunoreactivity of several allergenic foods. However, enzyme treatment has high requirements for the specificity of different proteins, so there are limitations for enzyme application in the reduction of food immunoreactivity.

Combination of processing techniques

As discussed above, the application of a single processing technique may not show a significant effect on the reduction in the immunoreactivity of certain foods. The combinations between various processing technologies provide a new strategy for reducing the immunoreactivity of food (Ekezie, Cheng, and Sun 2018). Studies reported that no significant differences in peanut structure were observed after high-pressure treatment at room temperature or even at 80 °C (Van der Plancken et al. 2012). However, the combination of high pressure and enzymatic treatment could easily lose the protein structure of peanut allergens, and such conformational changes of peanut allergens may further induce their property modifications (Dong et al. 2011). Chung, Houska, and Reed (2013) found the combination of high pressure (500 Mpa) and polyphenol oxidase to have significantly reduced the content of major peanut allergens and the IgE binding capacity by two times compared to either polyphenol oxidase or high-pressure treatment alone. The reduction of allergenic capacity of peanut might be because high pressure can enhance the susceptibility of proteins/allergens in enzyme hydrolysis (Chung, Houska, and Reed 2013). In soy, a similar study found that high pressure associated with enzymatic hydrolysis treatment (*flavourzyme*) could

efficiently reduce the immunoreactivity of soy proteins. The hydrolysis processing was accelerated by the combination with high pressure, which in turn attributed to modifying the epitopes of allergens (Meinlschmidt et al. 2017).

The combination of high pressure and the high temperature was also applied to reduce the allergenic potential of food products. In milk, Kleber, Maier, and Hinrichs (2007) found the antigenicity of β -lg to have shown a downward trend under combination treatment of high pressure (200–600 Mpa) and high temperature (60–68 °C), while no significant differences were observed under high pressure or thermal treatment (Kleber, Maier, and Hinrichs 2007). In whey protein, the combination of microwave irradiation (MWI) and chymotrypsin hydrolysis improved the enzymatic hydrolysis of whey protein and reduced the residual antigenicity of the hydrolysates, which might be due to the conformation rearrangements of proteins induced by MWI treatment (Izquierdo et al. 2008; Porcelli et al. 1997).

Additionally, studies have reported that ultrasound combined with enzymatic hydrolysis or germination treatment showed a potential application in the reduction of food immunoreactivity. In peanut, Li et al. (2013) treated roasted peanut with ultrasound (0–2 h) and enzyme treatment (1–9 h with α -chymotrypsin or trypsin). The results found that ultrasound-enzymatic treatment not only significantly raised the amount of soluble peanut protein and lowered IgE binding of the peanut extracts but also eliminated two main allergens (Ara h 1, Ara h 2) in peanuts. This reduction in peanut immunoreactivity may be due to ultrasound-enzyme treatment to have cleaved the roasted peanut protein sequences at some epitopes. Similarly, Yang et al. (2015) treated soy seeds with ultrasound treatment at 0–300 W, and then germinate them for five days. The results showed IgE-binding capacity of soybean protein under ultrasound-germination treatment significantly decreased by 51% compared to the untreated samples, which might be due to the disruption or elimination of epitopes in proteins during the ultrasound and germination treatment. Likewise, Yu, Liu, et al. (2016a) germinated peanut kernel for three days and then treated them with high-intensity ultrasound at a frequency of 100 kHz. The results showed that allergenic proteins were degraded completely (Yu, Liu, et al. 2016a).

It can be seen that the immunoreactivity of milk is more difficult to be reduced than that of other food allergens like soy, peanut, and wheat. The combined treatment of high pressure and high temperature may not perform as effectively as the combination of high pressure and enzymatic hydrolysis. Besides, both enzyme combined ultrasound and enzyme combined high pressure show a potential effect in reducing food immunoreactivity. Therefore, the combination treatment generally shows a better performance in reducing food immunoreactivity compared to the single processing technique.

Conclusion and future trends

Food allergy as a global health issue is expected to be addressed by using some innovative non-thermal processing

techniques, such as high-pressure processing, pulsed light, cold plasma, ultrasound, fermentation, pulsed electric field, enzymatic hydrolysis treatment, and combination of them. As discussed above, these novel processing techniques showed potential applications in the reduction of food allergens to produce hypoallergenic foods for individuals with a history of food allergy. In comparison to every single treatment, the combination of processing has a better performance in most cases. Ultrasound contributes to making proteins more accessible to the action of other treatments, such as enzymatic hydrolysis or thermal processing, thus promoting the reduction of the immunoreactivity of some foods. Long-time fermentation is also recommended as an efficient processing approach reported by studies, but the optimal conditions are still needed to be investigated. The pulsed UV light, cold plasma, and enzymatic hydrolysis generally show polarized effects in various foods and might have the potential to be applied to specific food allergens. High-pressure processing and pulsed electric field have a less positive impact on the reduction of food immunoreactivity compared with other non-thermal treatments. Indeed, multiple food allergens typically can be reduced by altering sequential or conformational epitopes and even eliminating them at certain optimal conditions. Thus, to improve the efficiency in the reduction of food immunoreactivity, the optimization of processing conditions (e.g., duration, energy, frequency, and temperature) in each treatment is needed. Further, the immune responses of individuals with food allergy history to these processed or modified foods are unknown, and further clinical studies are still in need. To date, the best therapeutic strategy suggested by the doctors is to avoid exposure to allergenic foods or related food sources.

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References

- Anugu, A. K. 2009. Effect of pulsed UV lights and pulsed electric fields on selected isolated milk proteins and their allergenic properties. Doctoral diss., Alabama A & M University.
- Awad, T. S., H. A. Moharram, O. E. Shaltout, D. Asker, and M. M. Youssef. 2012. Applications of ultrasound in analysis, processing and quality control of food: A review. *Food Research International* 48 (2):410–27. doi: 10.1016/j.foodres.2012.05.004.
- Barre, A., G. Jacquet, C. Sordet, R. Culierrier, and P. Rougé. 2007. Homology modelling and conformational analysis of IgE-binding

- epitopes of Ara h 3 and other legumin allergens with a cupin fold from tree nuts. *Molecular Immunology* 44 (12):3243–55. doi: [10.1016/j.molimm.2007.01.023](https://doi.org/10.1016/j.molimm.2007.01.023).
- Besler, M., H. Steinhart, and A. Paschke. 2001. Stability of food allergens and allergenicity of processed foods. *Journal of Chromatography B: Biomedical Sciences and Applications* 756 (1–2): 207–28. doi: [10.1016/S0378-4347\(01\)00110-4](https://doi.org/10.1016/S0378-4347(01)00110-4).
- Bhat, Z. F., J. D. Morton, S. L. Mason, and A. E.-D. A. Bekhit. 2019a. Current and future prospects for the use of pulsed electric field in the meat industry. *Critical Reviews in Food Science and Nutrition* 59 (10):1660–74. doi: [10.1080/10408398.2018.1425825](https://doi.org/10.1080/10408398.2018.1425825).
- Bhat, Z. F., J. D. Morton, S. L. Mason, A. E.-D. A. Bekhit, and T. E. Mungue. 2019b. Pulsed electric field: Effect on in-vitro simulated gastrointestinal protein digestion of deer *Longissimus dorsi*. *Food Research International* 120:793–9. doi: [10.1016/j.foodres.2018.11.040](https://doi.org/10.1016/j.foodres.2018.11.040).
- Blázquez, A. B., and M. C. Berin. 2017. Microbiome and food allergy. *Translational Research* 179:199–203. doi: [10.1016/j.trsl.2016.09.003](https://doi.org/10.1016/j.trsl.2016.09.003).
- Boye, J. I. 2012. Food allergies in developing and emerging economies: Need for comprehensive data on prevalence rates. *Clinical and Translational Allergy* 2 (1):25. doi: [10.1186/2045-7022-2-25](https://doi.org/10.1186/2045-7022-2-25).
- Breiteneder, H., and E. Mills. 2005. Molecular mechanisms in allergy and clinical immunology. *Journal of Allergy and Clinical Immunology* 115 (1):14–23. doi: [10.1016/j.jaci.2004.10.022](https://doi.org/10.1016/j.jaci.2004.10.022).
- Burks, A. W., M. Tang, S. Sicherer, A. Muraro, P. A. Eigenmann, M. Ebisawa, A. Fiocchi, W. Chiang, K. Beyer, R. Wood, et al. 2012. ICON: Food allergy. *Journal of Allergy and Clinical Immunology* 129 (4):906–20. doi: [10.1016/j.jaci.2012.02.001](https://doi.org/10.1016/j.jaci.2012.02.001).
- Cabanillas, B., M. M. Pedrosa, J. Rodríguez, Á. González, M. Muzquiz, C. Cuadrado, J. F. Crespo, and C. Burbano. 2010. Effects of enzymatic hydrolysis on lentil allergenicity. *Molecular Nutrition & Food Research* 54 (9):1266–72. doi: [10.1002/mnfr.200900249](https://doi.org/10.1002/mnfr.200900249).
- Chen, H. L., H. Y. Mao, M. J. Cao, Q. F. Cai, W. J. Su, Y. X. Zhang, and G. M. Liu. 2013. Purification, physicochemical and immunological characterization of arginine kinase, an allergen of crayfish (*Procambarus clarkii*). *Food and Chemical Toxicology* 62:475–84. doi: [10.1016/j.fct.2013.09.014](https://doi.org/10.1016/j.fct.2013.09.014).
- Chizoba Ekezie, F.-G., J.-H. Cheng, and D.-W. Sun. 2018. Effects of mild oxidative and structural modifications induced by argon plasma on physicochemical properties of actomyosin from king prawn (*Litopenaeus vannamei*). *Journal of Agricultural and Food Chemistry* 66 (50):13285–94. doi: [10.1021/acs.jafc.8b05178](https://doi.org/10.1021/acs.jafc.8b05178).
- Choudhary, R., D. Gautam, G. Perez-Alvarado, and M. Kinsel. 2013. Effect of high intensity ultrasound treatment in reducing the allergenicity of isolated cow's milk and soy proteins. Presented during IFCON in CFTRI Mysore, December 18–21.
- Chung, S.-Y., M. Houska, and S. Reed. 2013. Reducing peanut allergens by high pressure combined with polyphenol oxidase. *High Pressure Research* 33 (4):813–21. doi: [10.1080/08957959.2013.828716](https://doi.org/10.1080/08957959.2013.828716).
- Chung, Y. H., J. H. Kwon, J. A. Jung, J. O. Lee, K. S. Lee, J. Y. Kim, K. M. Ahn, S. I. Lee, and C. H. Ryu. 2008a. Evaluating the allergenicity of soybean by the fermentation. *Pediatric Allergy Respiratory Disease* 18 (1):37–45.
- Chung, S. Y., W. Yang, and K. Krishnamurthy. 2008b. Effects of pulsed UV-light on peanut allergens in extracts and liquid peanut butter. *Journal of Food Science* 73 (5):C400–C404. doi: [10.1111/j.1750-3841.2008.00784.x](https://doi.org/10.1111/j.1750-3841.2008.00784.x).
- Cianferoni, A., and J. M. Spergel. 2009. Food allergy: Review, classification and diagnosis. *Allergy International* 58 (4):457–66. doi: [10.2332/allergolint.09-RAI-0138](https://doi.org/10.2332/allergolint.09-RAI-0138).
- Dasan, B. G., and I. H. Boyaci. 2018. Effect of cold atmospheric plasma on inactivation of *Escherichia coli* and physicochemical properties of apple, orange, tomato juices, and sour cherry nectar. *Food and Bioprocess Technology* 11 (2):334–43. doi: [10.1007/s11947-017-2014-0](https://doi.org/10.1007/s11947-017-2014-0).
- De Angelis, M., C. G. Rizzello, A. Fasano, M. G. Clemente, C. De Simone, M. Silano, M. De Vincenzi, I. Losito, and M. Gobbetti. 2006. VSL# 3 probiotic preparation has the capacity to hydrolyze gliadin polypeptides responsible for celiac sprue probiotics and gluten intolerance. *Biochimica et Biophysica Acta -Molecular Basis of Disease* 1762 (1):80–93.
- Dong, X., M. Zhao, J. Shi, B. Yang, J. Li, D. Luo, G. Jiang, and Y. Jiang. 2011. Effects of combined high-pressure homogenization and enzymatic treatment on extraction yield, hydrolysis and function properties of peanut proteins. *Innovative Food Science & Emerging Technologies* 12 (4):478–83. doi: [10.1016/j.ifset.2011.07.002](https://doi.org/10.1016/j.ifset.2011.07.002).
- Duan, C. C., A. L. Li, L. J. Yang, R. Zhao, W. G. Fan, and G. C. Huo. 2014. Comparison of immunomodulating properties of Beta-lactoglobulin and its hydrolysates. *Iranian Journal of Allergy, Asthma Immunology* 13 (1):26–32.
- Ekezie, F. G. C., J. H. Cheng, and D. W. Sun. 2018. Effects of nonthermal food processing technologies on food allergens: A review of recent research advances. *Trends in Food Science & Technology* 74: 12–25. doi: [10.1016/j.tifs.2018.01.007](https://doi.org/10.1016/j.tifs.2018.01.007).
- Feng, H., G. V. Barbosa-Cánovas, and J. Weiss. 2011. *Ultrasound technologies for food and bioprocessing*. New York: Springer.
- Fleischer, D. M., C. Venter, and Y. Vandenplas. 2016. Hydrolyzed formula for every infant? In *Protein in neonatal and infant nutrition: Recent updates*, vol. 86, 51–65. Beijing: Karger Publishers.
- Forney, L. J., and C. I. Moraru. 2009. *Ultraviolet light in food technology: principles and applications*. Florida: CRC press.
- Gharbi, N., and M. Labbafi. 2018. Effect of processing on aggregation mechanism of egg white proteins. *Food Chemistry* 252:126–33. doi: [10.1016/j.foodchem.2018.01.088](https://doi.org/10.1016/j.foodchem.2018.01.088).
- Gupta, R., A. Sheikh, D. P. Strachan, and H. R. Anderson. 2007. Time trends in allergic disorders in the UK. *Thorax* 62 (1):91–6. doi: [10.1136/thx.2004.038844](https://doi.org/10.1136/thx.2004.038844).
- Han, Z., M. J. Cai, J. H. Cheng, and D. W. Sun. 2018. Effects of electric fields and electromagnetic wave on food protein structure and functionality: A review. *Trends in Food Science & Technology* 75:1–9. doi: [10.1016/j.tifs.2018.02.017](https://doi.org/10.1016/j.tifs.2018.02.017).
- Henderson, C. J., J. P. Abonia, E. C. King, P. E. Putnam, M. H. Collins, J. P. Franciosi, and M. E. Rothenberg. 2012. Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis. *Journal of Allergy and Clinical Immunology* 129 (6): 1570–8. doi: [10.1016/j.jaci.2012.03.023](https://doi.org/10.1016/j.jaci.2012.03.023).
- Inagaki, N. 2014. *Plasma surface modification and plasma polymerization*. Lancaster: CRC Press.
- Izquierdo, F. J., E. Peñas, M. L. Baeza, and R. Gomez. 2008. Effects of combined microwave and enzymatic treatments on the hydrolysis and immunoreactivity of dairy whey proteins. *International Dairy Journal* 18 (9):918–22. doi: [10.1016/j.idairyj.2008.01.005](https://doi.org/10.1016/j.idairyj.2008.01.005).
- Johnson, P. E., I. Van der Plancken, A. Balasa, F. A. Husband, T. Grauwet, M. Hendrickx, D. Knorr, E. C. Mills, and A. R. Mackie. 2010. High pressure, thermal and pulsed electric-field-induced structural changes in selected food allergens. *Molecular Nutrition & Food Research* 54 (12):1701–10. doi: [10.1002/mnfr.201000006](https://doi.org/10.1002/mnfr.201000006).
- Kasera, R., A. Singh, S. Lavasa, K. N. Prasad, and N. Arora. 2015. Enzymatic hydrolysis: A method in alleviating legume allergenicity. *Food and Chemical Toxicology* 76:54–60. doi: [10.1016/j.fct.2014.11.023](https://doi.org/10.1016/j.fct.2014.11.023).
- Khan, M. U., I. Ahmed, H. Lin, Z. Li, J. Costa, I. Mafra, Y. Chen, and Y.-N. Wu. 2019. Potential efficacy of processing technologies for mitigating crustacean allergenicity. *Critical Reviews in Food Science and Nutrition* 59 (17):2807–30. doi: [10.1080/10408398.2018.1471658](https://doi.org/10.1080/10408398.2018.1471658).
- Kim, S. M., J. G. Park, H. Saeki, A. Nakamura, J. W. Lee, M. W. Byun, and D. H. Ahn. 2008. Changes in the Allergenicity of Saeujeot by Fermentation. *Food Science Biotechnology* 17 (5):919–24.
- Kiyota, K., M. Yoshimitsu, T. Satsuki-Murakami, K. Akutsu, K. Kajimura, and T. Yamano. 2017. Detection of the tomato allergen Sola l 1 and evaluation of its reactivity after heat and papain treatment. *Food and Agricultural Immunology* 28 (6):1450–9. doi: [10.1080/09540105.2017.1347914](https://doi.org/10.1080/09540105.2017.1347914).
- Kleber, N., S. Maier, and J. Hinrichs. 2007. Antigenic response of bovine β -lactoglobulin influenced by ultra-high pressure treatment and temperature. *Innovative Food Science & Emerging Technologies* 8 (1):39–45. doi: [10.1016/j.ifset.2006.05.001](https://doi.org/10.1016/j.ifset.2006.05.001).
- Knights, R. 1985. Processing and evaluation of the antigenicity of protein hydrolysates. *Clinical Disease Pediatrics Nutrition* 4:105–15.
- Kondo, Y., and A. Urisu. 2009. Oral allergy syndrome. *Allergy International* 58 (4):485–91. doi: [10.2332/allergolint.09-RAI-0136](https://doi.org/10.2332/allergolint.09-RAI-0136).

- Krishnamurthy, K., A. Demirci, and J. Irudayaraj. 2007. Inactivation of *Staphylococcus aureus* in milk using flow-through pulsed UV-light treatment system. *Journal of Food Science* 72 (7):M233–M239. doi: [10.1111/j.1750-3841.2007.00438.x](https://doi.org/10.1111/j.1750-3841.2007.00438.x).
- Krishnamurthy, K., J. Irudayaraj, A. Demirci, and W. Yang. 2008. 11 UV pasteurization of food materials. *Food Processing Operations Modeling: Design Analysis* 107: 281.
- Kulis, M., I. MacQueen, Y. Li, R. Guo, X.-P. Zhong, and A. W. Burks. 2012. Pepsinized cashew proteins are hypoallergenic and immunogenic and provide effective immunotherapy in mice with cashew allergy. *Journal of Allergy and Clinical Immunology* 130 (3):716–23. doi: [10.1016/j.jaci.2012.05.044](https://doi.org/10.1016/j.jaci.2012.05.044).
- Kurpiewska, K., A. Biela, J. I. Loch, J. Lipowska, M. Siuda, and K. Lewiński. 2019. Towards understanding the effect of high pressure on food protein allergenicity: β -lactoglobulin structural studies. *Food Chemistry* 270:315–21. doi: [10.1016/j.foodchem.2018.07.104](https://doi.org/10.1016/j.foodchem.2018.07.104).
- Lasekan, A. O., and B. Nayak. 2016. Effects of buffer additives and thermal processing methods on the solubility of shrimp (*Penaeus monodon*) proteins and the immunoreactivity of its major allergen. *Food Chemistry* 200:146–53. doi: [10.1016/j.foodchem.2016.01.015](https://doi.org/10.1016/j.foodchem.2016.01.015).
- Lee, J. W., J. H. Kim, H. S. Yook, K. O. Kang, S. Y. Lee, H. J. Hwang, and M. W. Byun. 2001. Effects of gamma radiation on the allergenic and antigenic properties of milk proteins. *Journal of Food Protection* 64 (2):272–6. doi: [10.4315/0362-028X-64.2.272](https://doi.org/10.4315/0362-028X-64.2.272).
- Leszczyńska, J., A. Diowksz, A. Łącka, M. Bryszewska, K. Wolska, and W. Ambroziak. 2009. Decrease of wheat flour allergenicity via lactic acid fermentation. *Food and Agricultural Immunology* 20 (2):139–45. doi: [10.1080/09540100902889944](https://doi.org/10.1080/09540100902889944).
- Li, H., J. Yu, M. Ahmedna, and I. Goktepe. 2013. Reduction of major peanut allergens Ara h 1 and Ara h 2, in roasted peanuts by ultrasound assisted enzymatic treatment. *Food Chemistry* 141 (2):762–8. doi: [10.1016/j.foodchem.2013.03.049](https://doi.org/10.1016/j.foodchem.2013.03.049).
- Li, H., Y. Jia, W. Peng, K. Zhu, H. Zhou, and X. Guo. 2018. High hydrostatic pressure reducing allergenicity of soy protein isolate for infant formula evaluated by ELISA and proteomics via Chinese soy-allergic children's sera. *Food Chemistry* 269:311–7. doi: [10.1016/j.foodchem.2018.07.001](https://doi.org/10.1016/j.foodchem.2018.07.001).
- Li, X., Z. Li, H. Lin, and H. Samee. 2011. Effect of power ultrasound on the immunoactivity and texture changes of shrimp (*Penaeus vannamei*). *Czech Journal of Food Sciences* 29 (5):508–14. doi: [10.17221/242/2009-CJFS](https://doi.org/10.17221/242/2009-CJFS).
- Li, Y., J. Yu, I. Goktepe, and M. Ahmedna. 2016. The potential of papain and alcalase enzymes and process optimizations to reduce allergenic gliadins in wheat flour. *Food Chemistry* 196:1338–45. doi: [10.1016/j.foodchem.2015.10.089](https://doi.org/10.1016/j.foodchem.2015.10.089).
- Li, Z. X., H. Lin, L. M. Cao, and K. Jameel. 2006. Effect of high intensity ultrasound on the allergenicity of shrimp. *Journal of Zhejiang University Science B* 7 (4):251–6. doi: [10.1631/jzus.2006.B0251](https://doi.org/10.1631/jzus.2006.B0251).
- Manzocco, L., A. Panozzo, and M. C. Nicoli. 2012. Effect of ultraviolet processing on selected properties of egg white. *Food Chemistry* 135 (2):522–7. doi: [10.1016/j.foodchem.2012.05.028](https://doi.org/10.1016/j.foodchem.2012.05.028).
- Matricardi, P. M., J. Kleine-Tebbe, H. J. Hoffmann, R. Valenta, C. Hilger, S. Hofmaier, R. C. Aalberse, I. Agache, R. Asero, B. Ballmer-Weber, et al. 2016. EAACI molecular allergology user's guide. *Pediatric Allergy and Immunology* 27:1–250.
- Matsuoka, H., T. Yokooji, and T. Taogoshi. 2015. Common food allergens and their IgE-binding epitopes. *Allergology International* 64 (4): 332–43. doi: [10.1016/j.alit.2015.06.009](https://doi.org/10.1016/j.alit.2015.06.009).
- Meda, V., V. Orsat, and V. Raghavan. 2017. Microwave heating and the dielectric properties of foods. In *The microwave processing of foods*, 23–43. 2nd ed. Cambridge: Elsevier.
- Meinlschmidt, P., E. Ueberham, J. Lehmann, K. Reineke, O. Schlüter, U. Schweiggert-Weisz, and P. Eisner. 2016. The effects of pulsed ultraviolet light, cold atmospheric pressure plasma, and gamma-irradiation on the immunoreactivity of soy protein isolate. *Innovative Food Science & Emerging Technologies* 38:374–83. doi: [10.1016/j.ifset.2016.06.007](https://doi.org/10.1016/j.ifset.2016.06.007).
- Meinlschmidt, P., V. Brode, R. Sevenich, E. Ueberham, U. Schweiggert-Weisz, J. Lehmann, C. Rauh, D. Knorr, and P. Eisner. 2017. High pressure processing assisted enzymatic hydrolysis-An innovative approach for the reduction of soy immunoreactivity. *Innovative Food Science & Emerging Technologies* 40:58–67. doi: [10.1016/j.ifset.2016.06.022](https://doi.org/10.1016/j.ifset.2016.06.022).
- Meng, X., Y. Bai, J. Gao, X. Li, and H. Chen. 2017. Effects of high hydrostatic pressure on the structure and potential allergenicity of the major allergen bovine β -lactoglobulin. *Food Chemistry* 219: 290–6. doi: [10.1016/j.foodchem.2016.09.153](https://doi.org/10.1016/j.foodchem.2016.09.153).
- Metcalfe, D. D., H. A. Sampson, and R. A. Simon. 2011. *Food allergy: adverse reactions to foods and food additives*. Malden: Wiley-Blackwell.
- Misra, N., B. Tiwari, K. Raghavarao, and P. Cullen. 2011. Nonthermal plasma inactivation of food-borne pathogens. *Food Engineering Reviews* 3 (3–4):159–70. doi: [10.1007/s12393-011-9041-9](https://doi.org/10.1007/s12393-011-9041-9).
- Muntean, M.-V., O. Marian, V. Barbieru, G. M. Cătușescu, O. Ranta, I. Drocas, and S. Terhes. 2016. High pressure processing in food industry-characteristics and applications. *Agriculture and Agricultural Science Procedia* 10:377–83. doi: [10.1016/j.aaspro.2016.09.077](https://doi.org/10.1016/j.aaspro.2016.09.077).
- Nan, J., M. Zou, H. Wang, C. Xu, J. Zhang, B. Wei, L. He, and Y. Xu. 2018. Effect of ultra-high pressure on molecular structure and properties of bullfrog skin collagen. *International Journal of Biological Macromolecules* 111:200–7. doi: [10.1016/j.ijbiomac.2017.12.163](https://doi.org/10.1016/j.ijbiomac.2017.12.163).
- Nooji, J. K. 2011. *Reduction of wheat allergen potency by pulsed ultra-violet light, high hydrostatic pressure, and non-thermal plasma*. Florida: University of Florida.
- Palosuo, K., E. Varjonen, J. Nurkkala, N. Kalkkinen, R. Harvima, T. Reunala, and H. Alenius. 2003. Transglutaminase-mediated cross-linking of a peptic fraction of ω -5 gliadin enhances IgE reactivity in wheat-dependent, exercise-induced anaphylaxis. *Journal of Allergy and Clinical Immunology* 111 (6):1386–92. doi: [10.1067/mai.2003.1498](https://doi.org/10.1067/mai.2003.1498).
- Panda, R., A. O. Tetteh, S. N. Pramod, and R. E. Goodman. 2015. Enzymatic hydrolysis does not reduce the biological reactivity of soybean proteins for all allergic subjects. *Journal of Agricultural and Food Chemistry* 63 (43):9629–39. doi: [10.1021/acs.jafc.5b02927](https://doi.org/10.1021/acs.jafc.5b02927).
- Pankaj, S., Z. Wan, and K. Keener. 2018. Effects of cold plasma on food quality: A review. *Foods* 7 (1):4.
- Paschke, A. 2009. Aspects of food processing and its effect on allergen structure. *Molecular Nutrition & Food Research* 53 (8):959–62. doi: [10.1002/mnfr.200800187](https://doi.org/10.1002/mnfr.200800187).
- Pawankar, R., G. Canonica, S. Holgate, R. Lockey, and M. Blaiss. 2013. *World Allergy Organisation (WAO) white book on allergy: Update 2013*. Milwaukee: World Allergy Organization.
- Pérez Díaz, I. M., E. G. Altuntas, and V. K. Juneja. 2017. Microbial fermentation in food preservation. In *Microbial control and food preservation*, 281–98. New York: Springer.
- Polloni, L., A. DunnGalvin, E. Ferruzza, R. Bonaguro, F. Lazzarotto, A. Toniolo, N. Celegato, and A. Muraro. 2017. Coping strategies, alexithymia and anxiety in young patients with food allergy. *Allergy* 72 (7):1054–60. doi: [10.1111/all.13097](https://doi.org/10.1111/all.13097).
- Porcelli, M., G. Cacciapuoti, S. Fusco, R. Massa, G. d'Ambrosio, C. Bertoldo, M. De Rosa, and V. Zappia. 1997. Non-thermal effects of microwaves on proteins: Thermophilic enzymes as model system. *FEBS Letters* 402 (2–3):102–6. doi: [10.1016/S0014-5793\(96\)01505-0](https://doi.org/10.1016/S0014-5793(96)01505-0).
- Price, A., S. Ramachandran, G. P. Smith, M. L. Stevenson, M. K. Pomeranz, and D. E. Cohen. 2015. Oral allergy syndrome (pollen-food allergy syndrome). *Dermatitis* 26 (2):78–88. doi: [10.1097/DER.0000000000000087](https://doi.org/10.1097/DER.0000000000000087).
- Purohit-Sheth, T. S., and W. W. Carr. 2005. Oral allergy syndrome (pollen-food allergy syndrome). *Allergy and Asthma Proceedings* 26 (3):229–30.
- Radauer, C., and H. Breiteneder. 2007. Evolutionary biology of plant food allergens. *Journal of Allergy and Clinical Immunology* 120 (3): 518–25. doi: [10.1016/j.jaci.2007.07.024](https://doi.org/10.1016/j.jaci.2007.07.024).
- Rahaman, T., T. Vasiljevic, and L. Ramchandran. 2016. Effect of processing on conformational changes of food proteins related to allergenicity. *Trends in Food Science & Technology* 49:24–34. doi: [10.1016/j.tifs.2016.01.001](https://doi.org/10.1016/j.tifs.2016.01.001).

- Regier, M., and H. Schubert. 2005. Introducing microwave processing of food: Principles and technologies. In *The microwave processing of foods*, 3–20. Boca Raton: CRC Press.
- Rindsjö, E., and A. Scheynius. 2010. Mechanisms of IgE-mediated allergy. *Experimental Cell Research* 316 (8):1384–9. doi: [10.1016/j.yexcr.2010.02.038](https://doi.org/10.1016/j.yexcr.2010.02.038).
- Sampson, H. A. 2003. 9. Food allergy. *Journal of Allergy and Clinical Immunology* 111 (2):S540–S547. doi: [10.1067/mai.2003.134](https://doi.org/10.1067/mai.2003.134).
- Shriver, S. K. 2011. *Effect of selected nonthermal processing methods on the allergen reactivity of Atlantic white shrimp (Litopenaeus setiferus)*. Florida: University of Florida.
- Shriver, S. K., and W. W. Yang. 2011. Thermal and nonthermal methods for food allergen control. *Food Engineering Reviews* 3 (1):26–43. doi: [10.1007/s12393-011-9033-9](https://doi.org/10.1007/s12393-011-9033-9).
- Shriver, S., W. Yang, S. Y. Chung, and S. Percival. 2011. Pulsed ultraviolet light reduces immunoglobulin E binding to Atlantic white shrimp (*Litopenaeus setiferus*) extract. *International Journal of Environmental Research and Public Health* 8 (7):2569–83. doi: [10.3390/ijerph8072569](https://doi.org/10.3390/ijerph8072569).
- Sicherer, S. H., and H. Sampson. 2010. Food allergy. *Journal of Allergy and Clinical Immunology* 125 (2):S116–S125. doi: [10.1016/j.jaci.2009.08.028](https://doi.org/10.1016/j.jaci.2009.08.028).
- Sloane, D., and A. Sheffer. 2001. Oral allergy syndrome. In *Allergy and Asthma Proceedings*, vol. 22, 321–325. East Providence: OceanSide Publications.
- Socol, C. R., A. Pandey, and C. Larroche. 2013. *Fermentation processes engineering in the food industry*. Boca Raton, FL: CRC Press.
- Soria, A. C., and M. Villamiel. 2010. Effect of ultrasound on the technological properties and bioactivity of food: A review. *Trends in Food Science & Technology* 21 (7):323–31. doi: [10.1016/j.tifs.2010.04.003](https://doi.org/10.1016/j.tifs.2010.04.003).
- Stanic-Vucinic, D., M. Stojadinovic, M. Atanaskovic Markovic, J. Ognjenovic, H. Grönlund, M. van Hage, R. Lantto, A. I. Sancho, and T. C. Velickovic. 2012. Structural changes and allergenic properties of β -lactoglobulin upon exposure to high-intensity ultrasound. *Molecular Nutrition & Food Research* 56 (12):1894–905. doi: [10.1002/mnfr.201200179](https://doi.org/10.1002/mnfr.201200179).
- Tammineedi, C. V., R. Choudhary, G. C. Perez-Alvarado, and D. G. Watson. 2013. Determining the effect of UV-C, high intensity ultrasound and nonthermal atmospheric plasma treatments on reducing the allergenicity of α -casein and whey proteins. *Lwt - Food Science and Technology* 54 (1):35–41. doi: [10.1016/j.lwt.2013.05.020](https://doi.org/10.1016/j.lwt.2013.05.020).
- Thomas, K., C. Herouet-Guichene, G. Ladics, G. Bannon, A. Cockburn, R. Crevel, J. Fitzpatrick, C. Mills, L. Privalle, and S. Vieths. 2007. Evaluating the effect of food processing on the potential human allergenicity of novel proteins: International workshop report. *Food and Chemical Toxicology* 45 (7):1116–22. doi: [10.1016/j.fct.2006.12.016](https://doi.org/10.1016/j.fct.2006.12.016).
- Tolouie, H., M. A. Mohammadifar, H. Ghomi, and M. Hashemi. 2018. Cold atmospheric plasma manipulation of proteins in food systems. *Critical Reviews in Food Science and Nutrition* 58 (15):2583–97. doi: [10.1080/10408398.2017.1335689](https://doi.org/10.1080/10408398.2017.1335689).
- Van der Plancken, I., L. Verbeyst, K. De Vleeschouwer, T. Grauwet, R.-L. Heiniö, F. A. Husband, M. Lille, A. R. Mackie, A. Van Loey, and K. Viljanen. 2012. (Bio) chemical reactions during high pressure/high temperature processing affect safety and quality of plant-based foods. *Trends in Food Science & Technology* 23 (1):28–38. doi: [10.1016/j.tifs.2011.08.004](https://doi.org/10.1016/j.tifs.2011.08.004).
- Van Oort, M. 2009. Enzymes in food technology-introduction. *Enzymes in Food Technology*, 1–17. Chichester: Wiley-Blackwell.
- Vanga, S. K., A. Singh, and V. Raghavan. 2015. Effect of thermal and electric field treatment on the conformation of Ara h 6 peanut protein allergen. *Innovative Food Science & Emerging Technologies* 30: 79–88. doi: [10.1016/j.ifset.2015.03.003](https://doi.org/10.1016/j.ifset.2015.03.003).
- Vanga, S. K., A. Singh, and V. Raghavan. 2017. Review of conventional and novel food processing methods on food allergens. *Critical Reviews in Food Science and Nutrition* 57 (10):2077–94. doi: [10.1080/10408398.2015.1045965](https://doi.org/10.1080/10408398.2015.1045965).
- Vanga, S. K., A. Singh, F. Kalkan, Y. Garipey, V. Orsat, and V. Raghavan. 2016. Effect of thermal and high electric fields on secondary structure of Peanut protein. *International Journal of Food Properties* 19 (6):1259–71. doi: [10.1080/10942912.2015.1071841](https://doi.org/10.1080/10942912.2015.1071841).
- Venkatratnam, H., C. Sarangapani, O. Cahill, and C. B. Ryan. 2019. Effect of cold plasma treatment on the antigenicity of peanut allergen Ara h 1. *Innovative Food Science & Emerging Technologies* 52: 368–75. doi: [10.1016/j.ifset.2019.02.001](https://doi.org/10.1016/j.ifset.2019.02.001).
- Wang, J., S. K. Vanga, C. McCusker, and V. Raghavan. 2019. A Comprehensive Review on Kiwifruit Allergy: Pathogenesis, Diagnosis, Management, and Potential Modification of Allergens Through Processing. *Comprehensive Reviews in Food Science and Food Safety* 18 (2): 500–513.
- Wei, J. N., X. A. Zeng, T. Tang, Z. Jiang, and Y. Y. Liu. 2018. Unfolding and nanotube formation of ovalbumin induced by pulsed electric field. *Innovative Food Science & Emerging Technologies* 45: 249–54. doi: [10.1016/j.ifset.2017.10.011](https://doi.org/10.1016/j.ifset.2017.10.011).
- Wu, J., L. Lin, and F. T. Chau. 2001. Ultrasound-assisted extraction of ginseng saponins from ginseng roots and cultured ginseng cells. *Ultrasonics Sonochemistry* 8 (4):347–52. doi: [10.1016/S1350-4177\(01\)00066-9](https://doi.org/10.1016/S1350-4177(01)00066-9).
- Wu, T.-C., T.-C. Tsai, C.-F. Huang, F.-Y. Chang, C.-C. Lin, I.-F. Huang, C.-H. Chu, B.-H. Lau, L. Wu, H.-J. Peng, et al. 2012. Prevalence of food allergy in Taiwan: A questionnaire-based survey. *Internal Medicine Journal* 42 (12):1310–5. doi: [10.1111/j.1445-5994.2012.02820.x](https://doi.org/10.1111/j.1445-5994.2012.02820.x).
- Xi, J., and M. He. 2018. High hydrostatic pressure (HHP) effects on antigenicity and structural properties of soybean β -conglycinin. *Journal of Food Science and Technology* 55 (2):630–7. doi: [10.1007/s13197-017-2972-2](https://doi.org/10.1007/s13197-017-2972-2).
- Yang, A., L. Zuo, Y. Cheng, Z. Wu, X. Li, P. Tong, and H. Chen. 2018. Degradation of major allergens and allergenicity reduction of soybean meal through solid-state fermentation with microorganisms. *Food & Function* 9 (3):1899–909. doi: [10.1039/C7FO01824J](https://doi.org/10.1039/C7FO01824J).
- Yang, H., J. Gao, A. Yang, and H. Chen. 2015. The ultrasound-treated soybean seeds improve edibility and nutritional quality of soybean sprouts. *Food Research International* 77:704–10. doi: [10.1016/j.foodres.2015.01.011](https://doi.org/10.1016/j.foodres.2015.01.011).
- Yang, W. W., N. R. Mwakatage, R. Goodrich-Schneider, K. Krishnamurthy, and T. M. Rababah. 2012. Mitigation of major peanut allergens by pulsed ultraviolet light. *Food and Bioprocess Technology* 5 (7):2728–38. doi: [10.1007/s11947-011-0615-6](https://doi.org/10.1007/s11947-011-0615-6).
- Yang, W. W., S. K. Shriver, S. Y. Chung, S. Percival, M. J. Correll, and T. M. Rababah. 2012. In vitro gastric and intestinal digestions of pulsed light-treated shrimp extracts. *Applied Biochemistry and Biotechnology* 166 (6):1409–22. doi: [10.1007/s12010-011-9534-2](https://doi.org/10.1007/s12010-011-9534-2).
- Yang, W. W., S.-Y. Chung, O. Ajayi, K. Krishnamurthy, K. Konan, and R. Goodrich-Schneider. 2010. Use of pulsed ultraviolet light to reduce the allergenic potency of soybean extracts. *International Journal of Food Engineering* 6 (3):doi: [10.2202/1556-3758.1876](https://doi.org/10.2202/1556-3758.1876).
- Yang, W., Z. Tu, H. Wang, L. Zhang, Y. Gao, X. Li, and M. Tian. 2017. Immunogenic and structural properties of ovalbumin treated by pulsed electric fields. *International Journal of Food Properties* 20 (sup3):S3164–S3176. doi: [10.1080/10942912.2017.1396479](https://doi.org/10.1080/10942912.2017.1396479).
- Yang, X., J. Sun, J. Tao, Y. Ma, J. Wei, and F. Long. 2017b. The allergenic potential of walnuts treated with high pressure and heat in a mouse model of allergy. *Innovative Food Science & Emerging Technologies* 39:165–70. doi: [10.1016/j.ifset.2016.12.001](https://doi.org/10.1016/j.ifset.2016.12.001).
- Yao, M., Y. Luo, J. Shi, Y. Zhou, Q. Xu, and Z. Li. 2014. Effects of fermentation by *Lactobacillus rhamnosus* GG on the antigenicity and allergenicity of four cows' milk proteins. *Food and Agricultural Immunology* 25 (4):545–55. doi: [10.1080/09540105.2013.852163](https://doi.org/10.1080/09540105.2013.852163).
- Yu, J., I. Goktepe, and M. Ahmedna. 2013. Enzymatic treatment of peanut butter to reduce the concentration of major peanut allergens. *International Journal of Food Science & Technology* 48 (6):1224–34. doi: [10.1111/ijfs.12081](https://doi.org/10.1111/ijfs.12081).
- Yu, J., M. Ahmedna, I. Goktepe, H. Cheng, and S. Maleki. 2011. Enzymatic treatment of peanut kernels to reduce allergen levels. *Food Chemistry* 127 (3):1014–22. doi: [10.1016/j.foodchem.2011.01.074](https://doi.org/10.1016/j.foodchem.2011.01.074).

- Yu, M., H. Liu, A. Shi, L. Liu, and Q. Wang. 2016. Preparation of resveratrol-enriched and poor allergic protein peanut sprout from ultrasound treated peanut seeds. *Ultrasonics Sonochemistry* 28: 334–40. doi: [10.1016/j.ultsonch.2015.08.008](https://doi.org/10.1016/j.ultsonch.2015.08.008).
- Yu, W., D. M. H. Freeland, and K. C. Nadeau. 2016. Food allergy: Immune mechanisms, diagnosis and immunotherapy. *Nature Reviews Immunology* 16 (12):751–65. doi: [10.1038/nri.2016.111](https://doi.org/10.1038/nri.2016.111).
- Zhang, Y., S. He, and B. K. Simpson. 2018. Enzymes in Food Bioprocessing—Novel food enzymes, applications, and related techniques. *Current Opinion in Food Science* 19:30–5. doi: [10.1016/j.cofs.2017.12.007](https://doi.org/10.1016/j.cofs.2017.12.007).
- Zhang, Z., X. Zhang, W. Chen, and P. Zhou. 2018. Conformation stability, in vitro digestibility and allergenicity of tropomyosin from shrimp (*Exopalaemon modestus*) as affected by high intensity ultrasound. *Food Chemistry* 245:997–1009. doi: [10.1016/j.foodchem.2017.11.072](https://doi.org/10.1016/j.foodchem.2017.11.072).
- Zhao, W., and R. Yang. 2008. Comparative study of inactivation and conformational change of lysozyme induced by pulsed electric fields and heat. *European Food Research and Technology* 228 (1):47–54. doi: [10.1007/s00217-008-0905-z](https://doi.org/10.1007/s00217-008-0905-z).
- Zhao, W., and R. Yang. 2009. Effect of high-intensity pulsed electric fields on the activity, conformation and self-aggregation of pepsin. *Food Chemistry* 114 (3):777–81. doi: [10.1016/j.foodchem.2008.10.016](https://doi.org/10.1016/j.foodchem.2008.10.016).
- Zhenxing, L., L. Caolimin, and K. Jamil. 2006. Reduction of allergenic properties of shrimp (*Penaeus Vannamei*) allergens by high intensity ultrasound. *European Food Research and Technology* 223 (5):639–44. doi: [10.1007/s00217-005-0246-0](https://doi.org/10.1007/s00217-005-0246-0).
- Zhou, H., C. Wang, J. Ye, H. Chen, R. Tao, and F. Cao. 2016a. Effects of high hydrostatic pressure treatment on structural, allergenicity, and functional properties of proteins from ginkgo seeds. *Innovative Food Science & Emerging Technologies* 34:187–95. doi: [10.1016/j.ifset.2016.02.001](https://doi.org/10.1016/j.ifset.2016.02.001).
- Zhou, H., C. Wang, J. Ye, R. Tao, H. Chen, and F. Cao. 2016. Effects of enzymatic hydrolysis assisted by high hydrostatic pressure processing on the hydrolysis and allergenicity of proteins from ginkgo seeds. *Food and Bioprocess Technology* 9 (5):839–48. doi: [10.1007/s11947-016-1676-3](https://doi.org/10.1007/s11947-016-1676-3).